

Amendments to the Claims:

This listing of claims will replace all prior versions, and listings, of the claims in the application:

Listing of Claims:

1-2. (Cancelled).

3. (Currently amended) ~~The method of claim 2 wherein said GRF analog is~~ A method of increasing muscle function in a subject, said method comprising administering to said subject a GRF analog of formula A:

X-GRF Peptide (A)

wherein;

the GRF peptide is a peptide of formula B;

A1-A2-Asp-Ala-Ile-Phe-Thr-A8-Ser-Tyr-Arg-Lys-A13-Leu-A15-Gln-Leu-A18-Ala-Arg-Lys-Leu-Leu-A24-A25-Ile-A27-A28-Arg-A30-R0 (B)

wherein,

A1 is Tyr or His;

A2 is Val or Ala;

A8 is Asn or Ser;

A13 is Val or Ile;

A15 is Ala or Gly;

A18 is Ser or Tyr;
A24 is Gln or His;
A25 is Asp or Glu;
A27 is Met, Ile or Nle
A28 is Ser or Asn;
A30 is a bond or amino acid sequence of 1 up to 15 residues; and

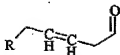
R0 is NH_2 or $\text{NH}-(\text{CH}_2)_n-\text{CONH}_2$, with $n=1$ to 12; and

X is a hydrophobic tail anchored via an amide bond to the N-terminus of the peptide and the hydrophobic tail defining a backbone of 5 to 7 atoms;

wherein the backbone can be substituted by C_{1-6} alkyl, C_{3-6} cycloalkyl, or C_{6-12} aryl and the backbone comprises at least one rigidifying moiety connected to at least two atoms of the backbone;

said moiety selected from the group consisting of double bond, triple bond, saturated or unsaturated C_{3-9} cycloalkyl, and C_{6-12} aryl.

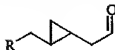
4. (Original) The method of claim 3, wherein X is selected from the group consisting of:



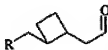
1 (R=H or CH₃ or CH₂CH₃)
cis or *trans*



2 (R=H or CH₃ or CH₂CH₃)



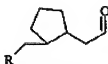
3 (R=H or CH₃ or CH₂CH₃)
cis or *trans*, both as racemic mixtures
or pure enantiomeric pairs



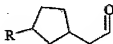
- 4 (R=H or CH₃ or CH₂CH₃)
cis or *trans*, both as racemic mixtures
or pure enantiomeric pairs



- 5 (R=H or CH₃ or CH₂CH₃)
cis or *trans*, (when R \neq H)



- 6 (R=H or CH₃ or CH₂CH₃)
cis or *trans*, both as racemic mixtures
or pure enantiomeric pairs



7 (R=H or CH₃ or CH₂CH₃)

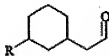
cis or *trans*, (when R \neq H)

both as racemic mixtures
or pure enantiomeric pairs



8 (R=H or CH₃ or CH₂CH₃)

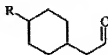
cis or *trans*, both as racemic mixtures
or pure enantiomeric pairs



9 (R=H or CH₃ or CH₂CH₃)

cis or *trans*, (when R ≠ H)

both as racemic mixtures
or pure enantiomeric pairs

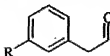


10 (R=H or CH₃ or CH₂CH₃)

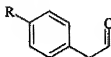
cis or *trans*, (when R ≠ H)



11 (R=H or CH₃ or CH₂CH₃)



12 (R=H or CH₃ or CH₂CH₃)



13 (R=H or CH₃ or CH₂CH₃)

and



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5. (Original) The method of claim 3, wherein A30 is selected from the group consisting of:
- (a) a bond;
 - (b) an amino acid sequence corresponding to positions 30-44 of a natural GRF peptide, and
 - (c) said amino acid sequence of (b) having a 1-14 amino acid deletion from its C-terminus.
6. (Original) The method of claim 3, wherein said GRF peptide is selected from the group consisting of:
- (a) a polypeptide comprising the amino acid sequence of SEQ ID NO: 3;
 - (b) a polypeptide comprising the amino acid sequence of SEQ ID NO: 5; and
 - (c) said polypeptide of (a) having a 1 to 14 amino acid deletion from its C-terminus.
7. (Currently amended) The method of claim 32, wherein said GRF analog is (hexenoyl trans-3)hGRF(1-44)NH₂ (SEQ ID NO: 7).
8. (Currently amended) The method of claim 31, wherein said muscle function is selected from the group consisting of:
- (a) muscle strength;
 - (b) muscle endurance; and
 - (c) both (a) and (b).

9. (Original) The method of claim 8, wherein said muscle function is muscle strength.
10. (Original) The method of claim 9, wherein said muscle strength is peripheral muscle strength.
11. (Original) The method of claim 8, wherein said muscle function is muscle endurance.
12. (Currently amended) The method of claim ~~31~~, wherein said increase results in a reduction of a parameter selected from the group consisting of:
 - (a) breathing discomfort;
 - (b) leg discomfort; and
 - (c) both (a) and (b).
13. (Currently amended) The method of claim ~~31~~, wherein said increase results in an increase in lean body mass in said subject.
14. (Currently amended) The method of claim ~~31~~, wherein said increase results in a decrease in fat mass in said subject.
15. (Currently amended) The method of claim ~~31~~, wherein the subject suffers from wasting.
16. (Original) The method of claim 15, wherein said wasting is associated with a condition selected from the group consisting of chronic obstructive pulmonary disease, chronic renal failure, congestive hear failure, human immunodeficiency virus infection, acquired immunodeficiency syndrome, cancer, malnutrition, frailty, immobilization paraplegia and spinal disorder.

17. (Currently amended) The method of claim 31, wherein said subject suffers from severe wasting.

18. (Original) The method of claim 17, wherein said subject has a body mass index less than or equal to 20.

19. (Original) The method of claim 17, wherein said subject has a weight less than 90% of ideal body weight.

20. (Original) The method of claim 17, wherein said subject is a male and said subject has a fat free mass index less than or equal to 16.

21. (Original) The method of claim 17, wherein said subject is a female and said subject has a fat free mass index less than or equal to 15.

22. (Currently amended) The method of claim 34, wherein said GRF analog~~agent~~ is administered through a route selected from the group consisting of intravenous, oral, transdermal, subcutaneous, mucosal, intramuscular, intranasal, intrapulmonary, parenteral, intrarectal and topical.

23. (Currently amended) The method of claim 34, wherein said GRF analog~~GH secretagogue~~ is administered in a dose from about 0.0001 mg to about 4 mg.

24. (Currently amended) The method of claim 234, wherein said GRF analog~~GH secretagogue~~ is administered in a dose selected from the group consisting of about 1 mg and about 2 mg.

25-49. (Canceled)

50. (Original) A package comprising:
- (i) an agent selected from the group consisting of:
 - (a) a growth hormone (GH) secretagogue; and
 - (b) a composition comprising a GH secretagogue and a pharmaceutically acceptable carrier; and
 - (ii) instructions for increasing muscle function in a subject.
51. (Original) The package of claim 50, wherein said GH secretagogue is selected from the group consisting of a GH-releasing factor (GRF) and a GRF analog.
52. (Original) The package of claim 51, wherein said GRF analog is a GRF analog of formula A:

X-GRF Peptide (A)

wherein;

the GRF peptide is a peptide of formula B;

A1-A2-Asp-Ala-Ile-Phe-Thr-A8-Ser-Tyr-Arg-Lys-A13-Leu-A15-Gln-Leu-A18-Ala-Arg-Lys-Leu-Leu-A24-A25-Ile-A27-A28-Arg-A30-R0 (B)

wherein,

A1 is Tyr or His;

A2 is Val or Ala;

A8 is Asn or Ser;

A13 is Val or Ile;

A15 is Ala or Gly;

A18 is Ser or Tyr;
A24 is Gln or His;
A25 is Asp or Glu;
A27 is Met, Ile or Nle
A28 is Ser or Asn;
A30 is a bond or amino acid sequence of 1 up to 15 residues; and

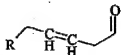
R0 is NH_2 or $\text{NH}-(\text{CH}_2)_n-\text{CONH}_2$, with $n=1$ to 12; and

X is a hydrophobic tail anchored via an amide bond to the N-terminus of the peptide and the hydrophobic tail defining a backbone of 5 to 7 atoms;

wherein the backbone can be substituted by C_{1-6} alkyl, C_{3-6} cycloalkyl, or C_{6-12} aryl and the backbone comprises at least one rigidifying moiety connected to at least two atoms of the backbone;

said moiety selected from the group consisting of double bond, triple bond, saturated or unsaturated C_{3-9} cycloalkyl, and C_{6-12} aryl.

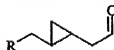
53. (Original) The package of claim 52, wherein X is selected from the group consisting of:



1 (R=H or CH_3 or CH_2CH_3)
cis or trans



2 (R=H or CH_3 or CH_2CH_3)



3 (R=H or CH_3 or CH_2CH_3)
cis or trans, both as racemic mixtures
or pure enantiomeric pairs



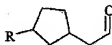
- 4 (R=H or CH₃ or CH₂CH₃)
cis or *trans*, both as racemic mixtures
or pure enantiomeric pairs



- 5 (R=H or CH₃ or CH₂CH₃)
cis or *trans*, (when R \neq H)



- 6 (R=H or CH₃ or CH₂CH₃)
cis or *trans*, both as racemic mixtures
or pure enantiomeric pairs



- 7 (R=H or CH₃ or CH₂CH₃)
cis or *trans*, (when R \neq H)
both as racemic mixtures
or pure enantiomeric pairs



- 8 (R=H or CH₃ or CH₂CH₃)
cis or *trans*, both as racemic mixtures
or pure enantiomeric pairs



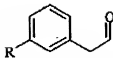
- 9 (R=H or CH₃ or CH₂CH₃)
cis or *trans*, (when R \neq H)
both as racemic mixtures
or pure enantiomeric pairs



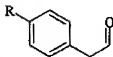
- 10 (R=H or CH₃ or CH₂CH₃)
cis or *trans*, (when R \neq H)



- 11 (R=H or CH₃ or CH₂CH₃)

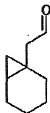


- 12 (R=H or CH₃ or CH₂CH₃)



- 13 (R=H or CH₃ or CH₂CH₃)

and



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54. (Original) The package of claim 52, wherein A30 is selected from the group consisting of:
- (a) a bond;
 - (b) an amino acid sequence corresponding to positions 30-44 of a natural GRF peptide, and
 - (c) said amino acid sequence of (b) having a 1-14 amino acid deletion from its C-terminus.
55. (Original) The package of claim 52, wherein said GRF peptide is selected from the group consisting of:
- (a) a polypeptide comprising the amino acid sequence of SEQ ID NO: 3;
 - (b) a polypeptide comprising the amino acid sequence of SEQ ID NO: 5; and
 - (c) said polypeptide of (a) having a 1 to 14 amino acid deletion from its C-terminus.
56. (Original) The package of claim 51, wherein said GRF analog is (hexenoyl trans-3)hGRF(1-44)NH₂ (SEQ ID NO: 7).
- 57-73. (Canceled)
74. (Original) A composition for increasing muscle function in a subject, said composition comprising:

- (a) a growth hormone (GH) secretagogue; and
 - (b) a pharmaceutically acceptable carrier.
75. (Original) The composition of claim 74, wherein said GH secretagogue is selected from the group consisting of a GH-releasing factor (GRF) and a GRF analog.
76. (Original) The composition of claim 75, wherein said GRF analog is a GRF analog of formula A:

X-GRF Peptide (A)

wherein;

the GRF peptide is a peptide of formula B;

A1-A2-Asp-Ala-Ile-Phe-Thr-A8-Ser-Tyr-Arg-Lys-A13-Leu-A15-Gln-Leu-A18-Ala-Arg-Lys-Leu-Leu-A24-A25-Ile-A27-A28-Arg-A30-R0 (B)

wherein,

A1 is Tyr or His;
A2 is Val or Ala;
A8 is Asn or Ser;
A13 is Val or Ile;
A15 is Ala or Gly;
A18 is Ser or Tyr;
A24 is Gln or His;
A25 is Asp or Glu;
A27 is Met, Ile or Nle

A28 is Ser or Asn;

A30 is a bond or amino acid sequence of 1 up to 15 residues; and

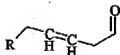
R0 is NH_2 or $\text{NH}-(\text{CH}_2)_n-\text{CONH}_2$, with $n=1$ to 12; and

X is a hydrophobic tail anchored via an amide bond to the N-terminus of the peptide and the hydrophobic tail defining a backbone of 5 to 7 atoms;

wherein the backbone can be substituted by C_{1-6} alkyl, C_{3-6} cycloalkyl, or C_{6-12} aryl and the backbone comprises at least one rigidifying moiety connected to at least two atoms of the backbone;

said moiety selected from the group consisting of double bond, triple bond, saturated or unsaturated C_{3-9} cycloalkyl, and C_{6-12} aryl.

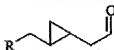
77. (Original) The composition of claim 76, wherein X is selected from the group consisting of:



1 (R=H or CH₃ or CH₂CH₃)
cis or trans



2 (R=H or CH₃ or CH₂CH₃)



3 (R=H or CH₃ or CH₂CH₃)
cis or trans, both as racemic mixtures
or pure enantiomeric pairs



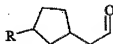
4 (R=H or CH₃ or CH₂CH₃)
cis or trans, both as racemic mixtures
or pure enantiomeric pairs



5 (R=H or CH₃ or CH₂CH₃)
cis or trans, (when R \neq H)



6 (R=H or CH₃ or CH₂CH₃)
cis or trans, both as racemic mixtures
or pure enantiomeric pairs



7 (R=H or CH₃ or CH₂CH₃)

cis or *trans*, (when R \neq H)

both as racemic mixtures
or pure enantiomeric pairs



8 (R=H or CH₃ or CH₂CH₃)

cis or *trans*, both as racemic mixtures
or pure enantiomeric pairs



9 (R=H or CH₃ or CH₂CH₃)

cis or *trans*, (when R \neq H)

both as racemic mixtures
or pure enantiomeric pairs

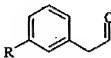


10 (R=H or CH₃ or CH₂CH₃)

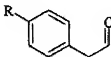
cis or *trans*, (when R \neq H)



11 (R=H or CH₃ or CH₂CH₃)



12 (R=H or CH₃ or CH₂CH₃)



13 (R=H or CH₃ or CH₂CH₃)

and



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78. (Original) The composition of claim 76, wherein A30 is selected from the group consisting of:
- (a) a bond;
 - (b) an amino acid sequence corresponding to positions 30-44 of a natural GRF peptide, and
 - (c) said amino acid sequence of (b) having a 1-14 amino acid deletion from its C-terminus.
79. (Original) The composition of claim 76, wherein said GRF peptide is selected from the group consisting of:
- (a) a polypeptide comprising the amino acid sequence of SEQ ID NO: 3;
 - (b) a polypeptide comprising the amino acid sequence of SEQ ID NO: 5; and

- (c) the polypeptide of (a) having a 1 to 14 amino acid deletion from its C-terminus.
80. (Original) The composition of claim 75, wherein said GRF analog is (hexenoyl trans 3)hGRF(1-44)NH₂ (SEQ ID NO: 7).